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Center for Genetics and Complex Traits
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CCEB



Why do Men of African Descent Have Unfavorable Prostate Cancer Outcomes?

A Transdisciplinary, Translational Approach

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Disparities in Cancer Mortality (Men)

Site	African American	European American	Ratio of African:European American
Prostate	62.3	25.6	2.4
Larynx	5.0	2.2	2.3
Stomach	11.9	5.2	2.3
Myeloma	8.5	4.4	1.9
Oral cavity and pharynx	6.8	3.8	1.8
Small intestine	0.7	0.4	1.8
Liver	10.0	6.5	1.5
Colon and rectum	32.7	22.9	1.4
Esophagus	10.2	7.7	1.3
Lung and bronchus	95.8	72.6	1.3
Pancreas	15.5	12.0	1.3

*Per 100,000, age-adjusted to the 2000 US standard population.

Source: Surveillance, Epidemiology, and End Results Program, 1975-2004, Division of Cancer Control and Population Sciences, National Cancer Institute, 2007.

CPHHD1 Research Framework

Neighborhood/
Community Context

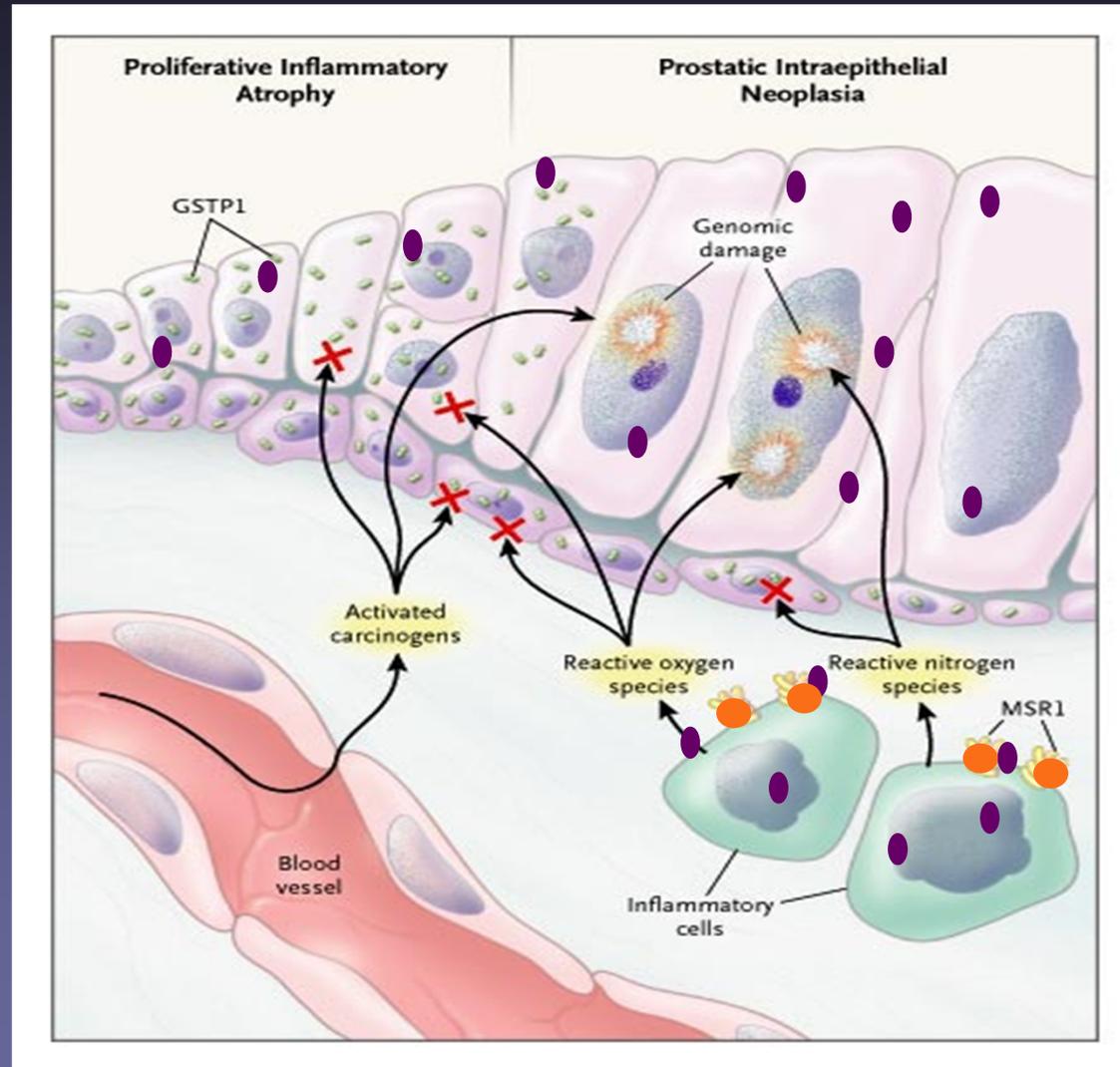
Community Engagement



2 Preclinical and Clinical Studies:
Screening, Treatment

3 Impact on Patient and Community:
Dissemination of Research, Quality of Life,
Access to Care, Policy

1. Molecular Events in Prostate Cancer



Nelson et al. *NEJM* 349:366, 2003

- **RNASEL** constitutively expressed latent endonuclease that mediates the antiviral activities of the interferon-inducible 2-5 A system

- **MSR1** Member of an extended family of scavenger receptors

1. Genotype, Neighborhood Context and PSA Failure

Neighborhood Dysregulation	Effect of <i>RNASEL</i> ivs7 indelTTA	Effect of <i>MSR1</i> R462Q
Lowest Tertile	0.72 (0.15-3.36)	No Failures
Middle Tertile	1.07 (0.17-6.81)	No Failures
Highest Tertile	9.40 (1.18-74.89)	3.27 (0.85-12.61)

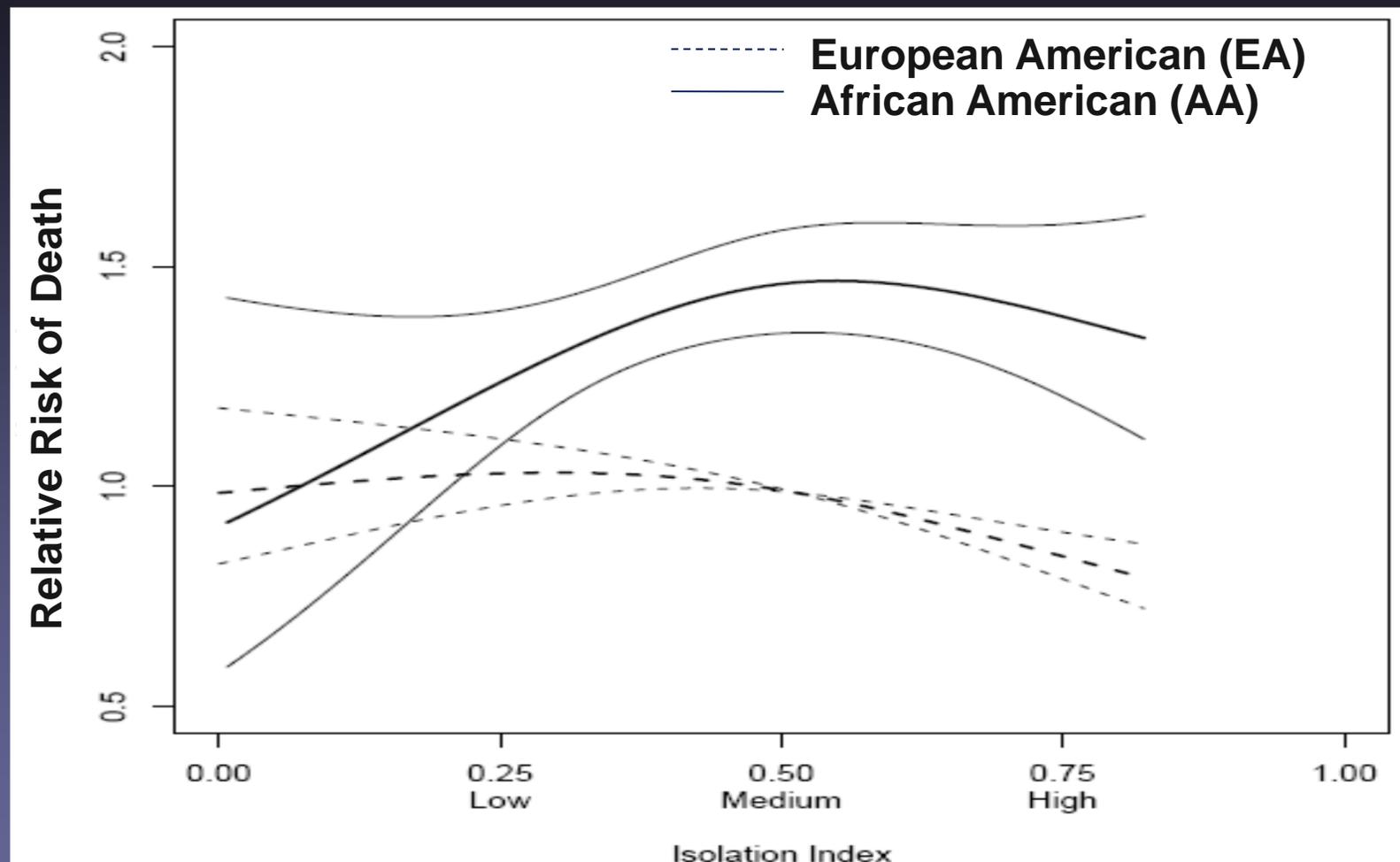
Lessons Learned:
Genotype Effects on Prostate Cancer Outcomes Depend on Context

2. Treatment and Mortality in Prostate Cancer (Wong et al. JAMA 2006)

Men >65	Untreated	Treated	Relative Risk of Death
European American	12,468 (25%)	36,907 (75%)	1.24
African American	1,071 (39%)	1,657 (61%)	1.37

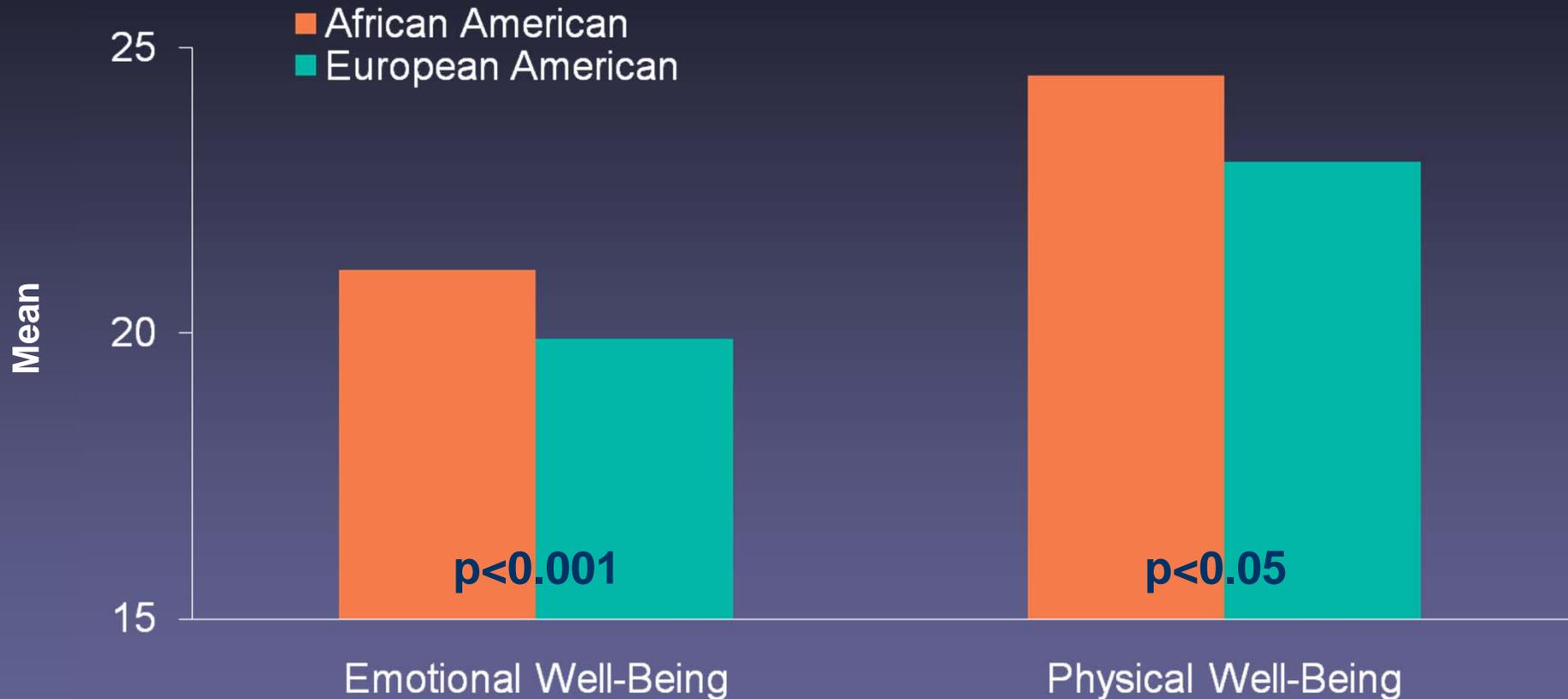
**Lessons Learned:
Unequal Application of Treatment by
Race Leads to Mortality Differences**

2. Prostate Cancer Mortality and Residential Segregation



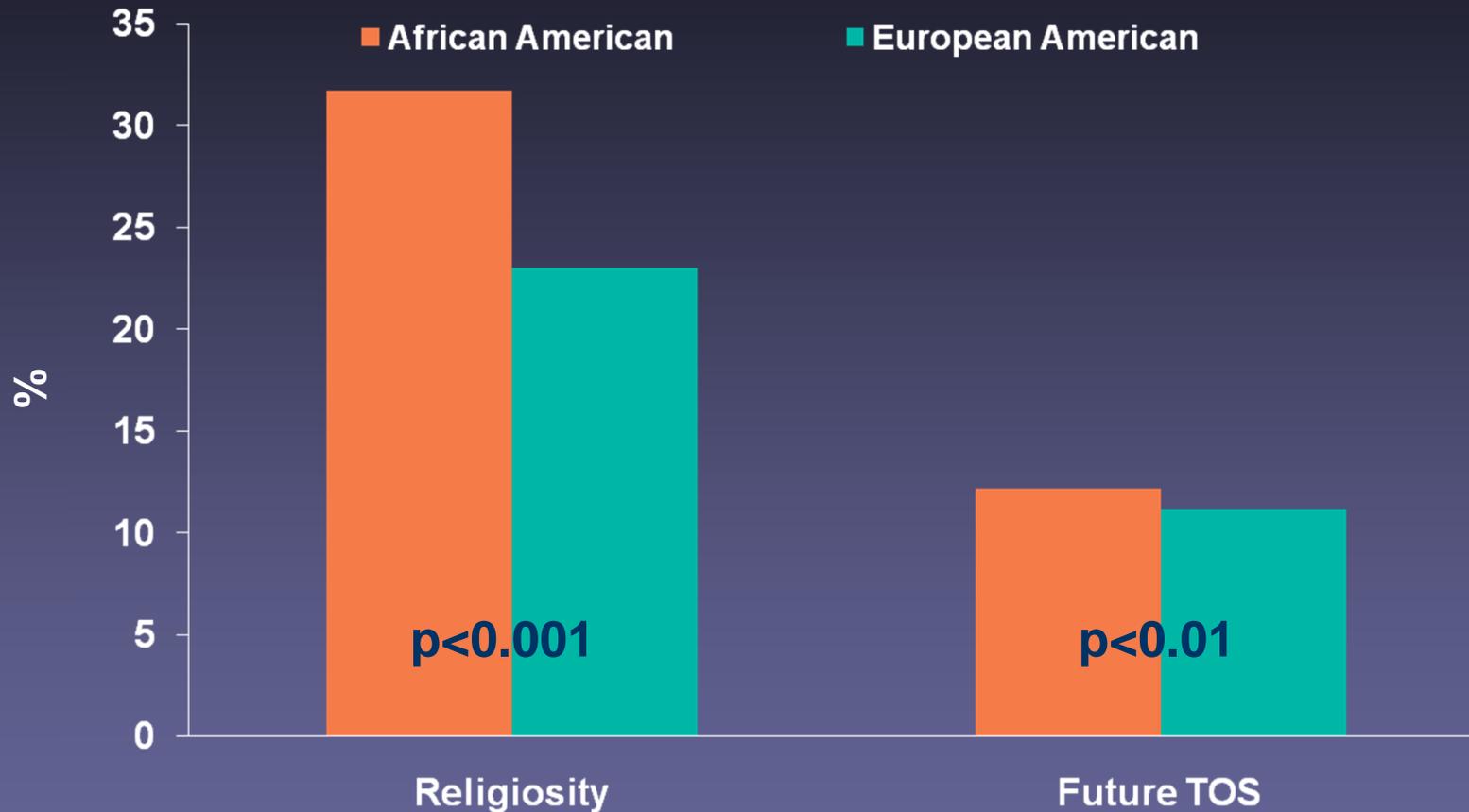
Lessons Learned:
**Residential Segregation Affects
EA and AA Men Differently**

3. Racial Differences in Quality of Life (Hughes-Halbert 2007)



**Lessons Learned:
Quality of Life May Affect Response
to Prostate Cancer Diagnosis**

3. Cultural Differences by Race (Hughes-Halbert 2008)

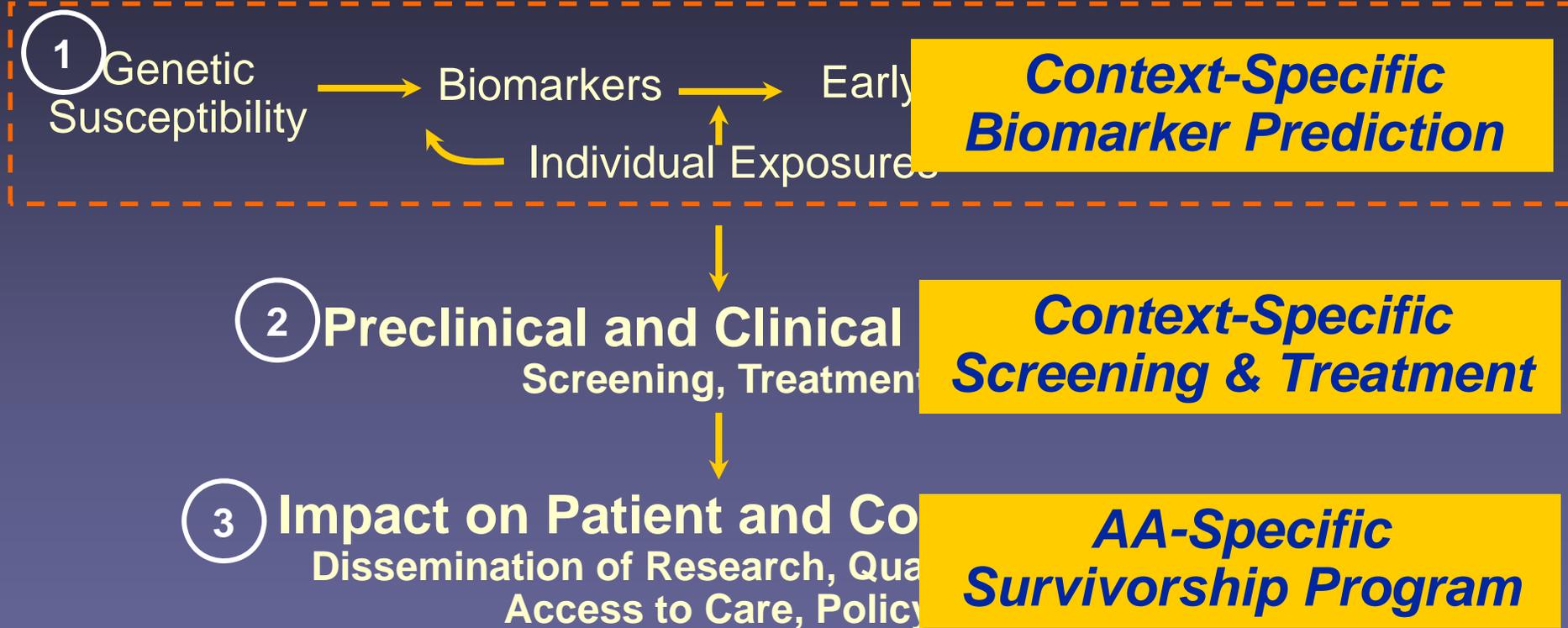


Lessons Learned:
***Survivorship Programs Require
Incorporation of Cultural Values***

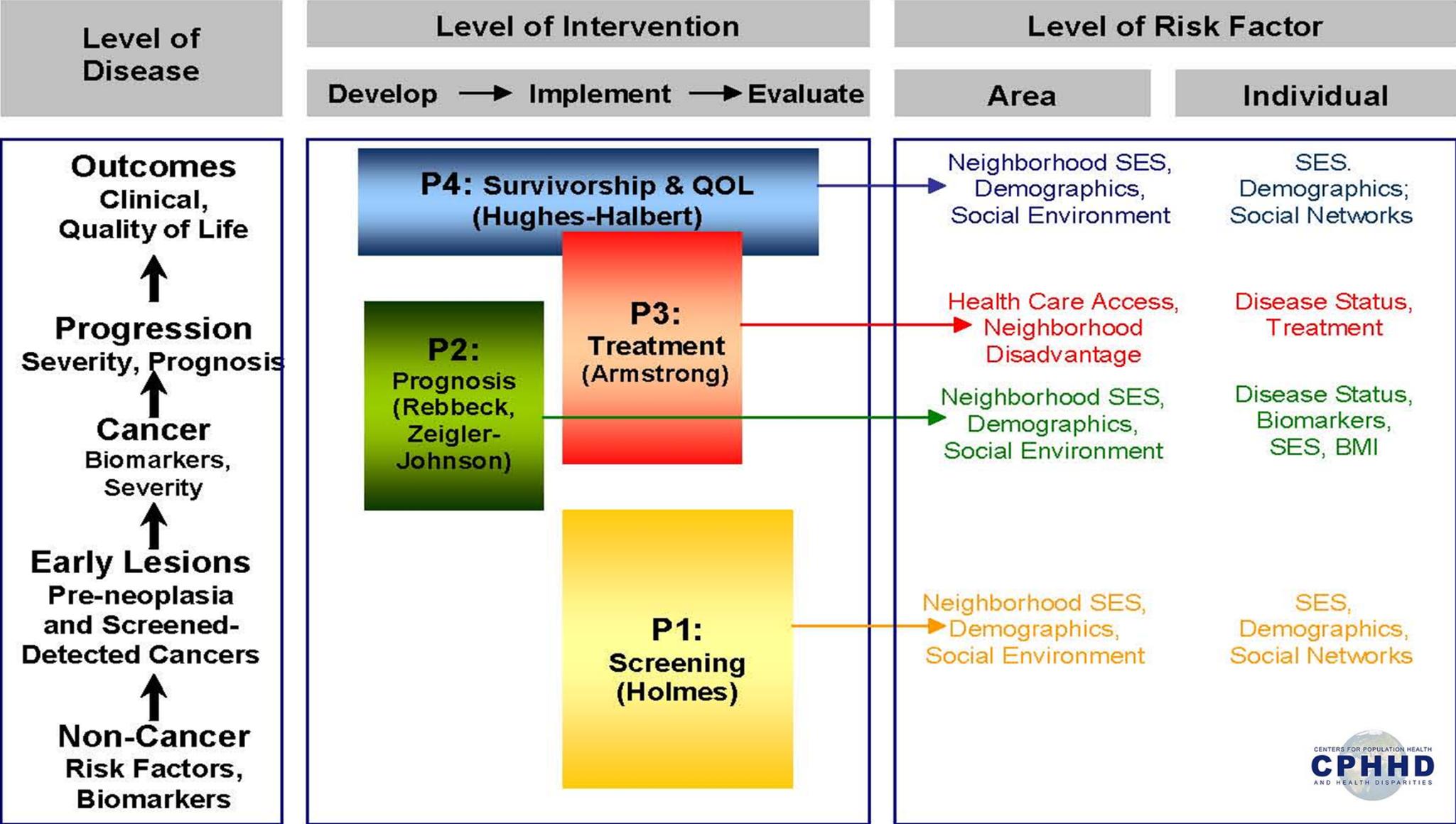
CPHHD2 Translation & Intervention

Neighborhood/
Community Context

Community Engagement



CPHHD2 Transdisciplinary, Translational Research Framework



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Cells to Society: Overcoming Health Disparities



How Are the CPHHDs Changing the Face of Health Disparities?

- **Emergence of Common Research Synergies and themes**
 - Genetic susceptibility and regulation of gene expression
 - Cumulative physiological dysregulation
 - Biological effects of a threatening social environment
 - Contextual effects of individual- and area-level factors
- **New Transdisciplinary Paradigm**
 - New research methods & tools
 - Comparative effectiveness research integrating biology, behavior, neighborhood, environment, and health care
 - Training, dissemination, and community engagement

Challenges and Opportunities for Eliminating Health Disparities

- **Novel transdisciplinary research**
 - Enhanced integration of disciplines
 - Maturation of emerging scientific themes
- **Develop and test comparative effectiveness interventions**
 - Exploit synergies of population health, biology, and personalized medicine
 - Targeted screening/prevention strategies
 - Novel therapies and applications of existing therapies
 - Optimize health care use
 - Policy impact

Questions for the NCAB

- How can the next phase of the CPHHD best be leveraged to more broadly engage the cancer and chronic disease communities to address health inequities?
- How can NCI best ensure that the state of the science concerning disparities informs policy making?
- Given that NHLBI is joining NCI on the CPHHD, what other opportunities might there be to synergize these areas of science (cancer and other chronic diseases including cardiovascular diseases) to address these problems.